

FIG. 1

ASSOCIATION STUDIES (FIRST SCREENING)

POPULATION SAMPLE SIZE	AFFECTED CASES= 112	NON AFFECTED CONTROLS=76
POPULATION CHARACTERISTICS	35 SPORADIC CASES +77 FAMILIAL CASES	>65 YEARS SA<4

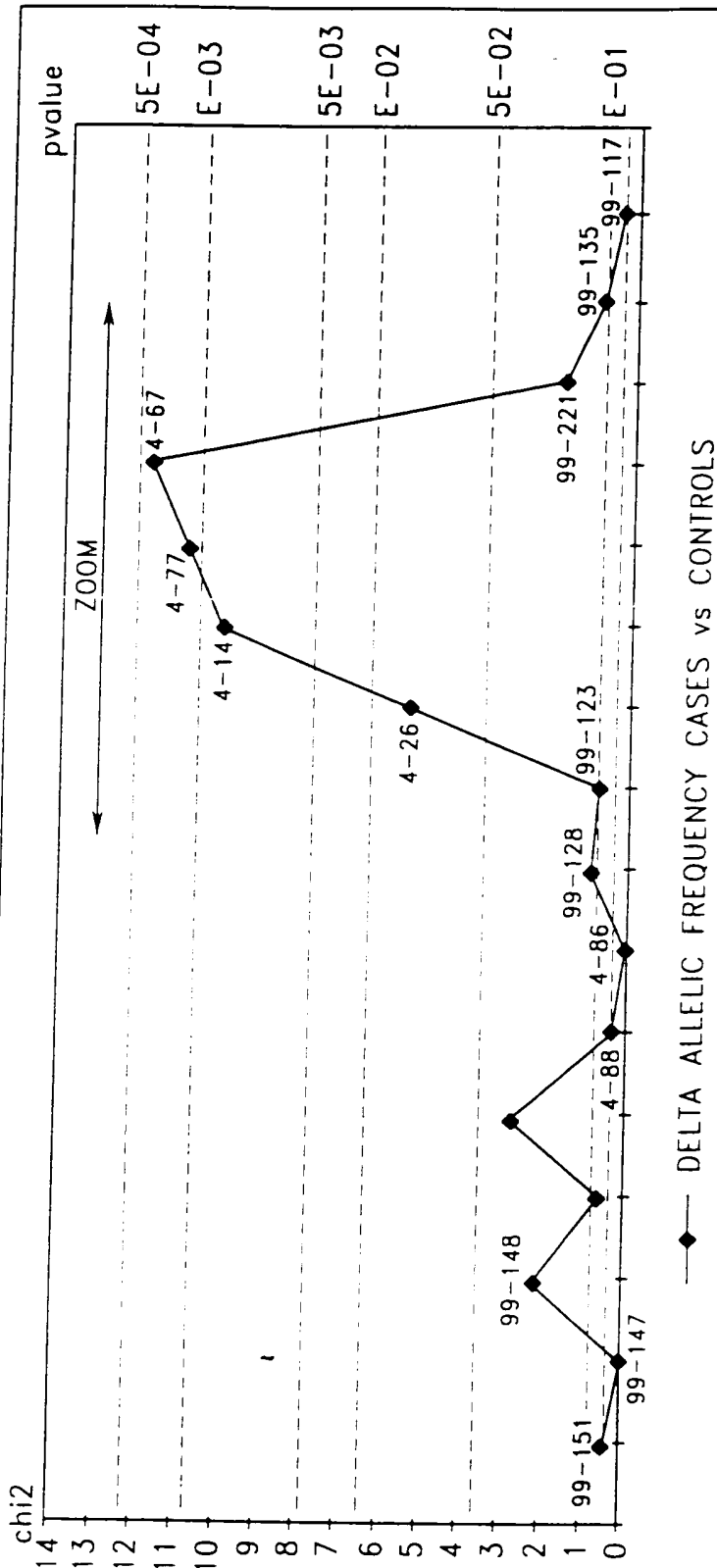


FIG.2

ASSOCIATION STUDIES (ZOOM)

CHARACTERISTICS OF POPULATIONS	AFFECTED CASES (185)	UNAFFECTED CONTROLS (104)
	47 SPORADIC CASES +138 FAMILIAL CASES	>65 YEARS P _{SA} <4

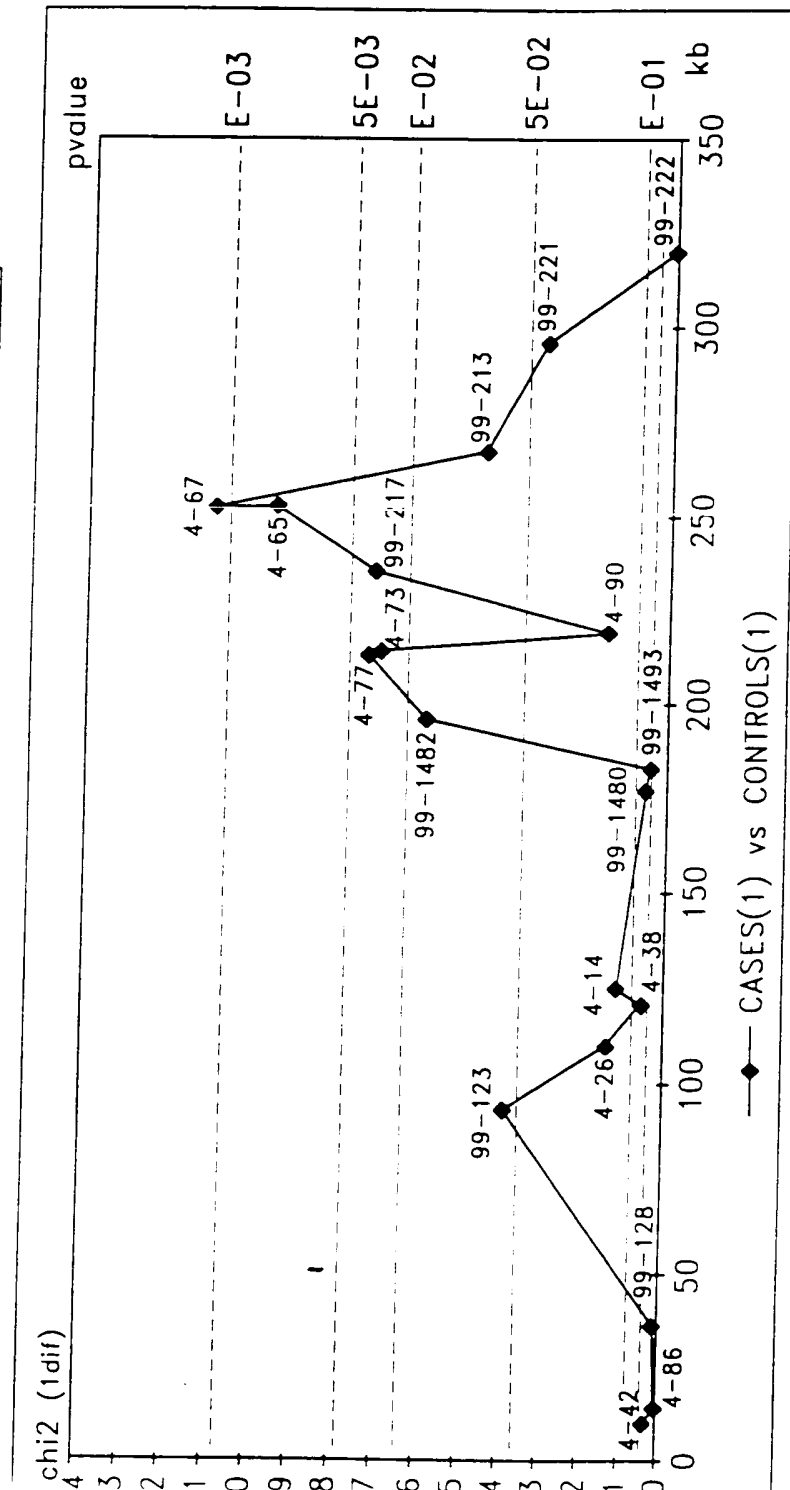


FIG.3

HAPLOTYPE FREQUENCY ANALYSIS

VARIATIONS

CHARACTERISTICS OF POPULATIONS	AFFECTED		UNAFFECTED	
	CASES 2 (281)	CONTROLS 3 (130)	>65 YEARS PSA<4	
143 SPORADIC CASES +138 FAMILIAL CASES				

MARKERS										HAPLOTYPE FREQUENCIES		RELATIVE RISK	PVALUE
										CASES (2)	CONTROLS (3)		
										B0463F01		B0725B12	
										11453			
										PG1			
VALUE													
E BETWEEN MARKERS(KB)													
OTYPE 8>304KB<	2,00E-01	1,00E-01	1,00E-01	2,00E-02	2,00E-02	5,00E-04	9,00E-02	7,00E-01	2,00E-01	0,075	0,018	4,42	9,00E-04 ***
OTYPE 7>286KB<		A	C	G	T	T	G	A	A	0,095	0,016	6,46	6,00E-05 ****
OTYPE 6<186KB>		A	C	G	T	T	G	A		0,116	0,019	6,78	1,00E-05*****
OTYPE 5<171KB>			C	G	T	T	G	A		0,117	0,013	10,06	9,00E-07*****
OTYPE 4<83KB>				G	T	T	G	A		0,117	0,025	5,17	2,00E-05*****
OTYPE 3.1<54KB>					T	T	G	A		0,117	0,027	4,78	2,00E-05*****
OTYPE 3.2<54KB>				G	T	T	G			0,222	0,109	2,33	4,00E-05*****
OTYPE 2.2<39KB>				G	T	T				0,251	0,134	2,17	2,00E-04****
OTYPE 2<32KB>					T	T	G			0,226	0,112	2,32	1,00E-04***
OTYPE 1.1<17KB>					T	T				0,256	0,146	2,01	3,00E-04****
OTYPE 1.2<15KB>						T	G			0,233	0,129	2,05	6,00E-04****

FIG.4

HAPLOTYPE SIMULATIONS (100 ITERATIONS)

MARKERS	HAPLOTYPE FREQUENCIES					RELATIVE RISK	PVALUE
	CASES		CONTROLS				
HAPLOTYPE	4-144-7799-2174-6799-21399-221	A	0,117	0,013		10,06	9,00E-07
	C	G	T	T	G		

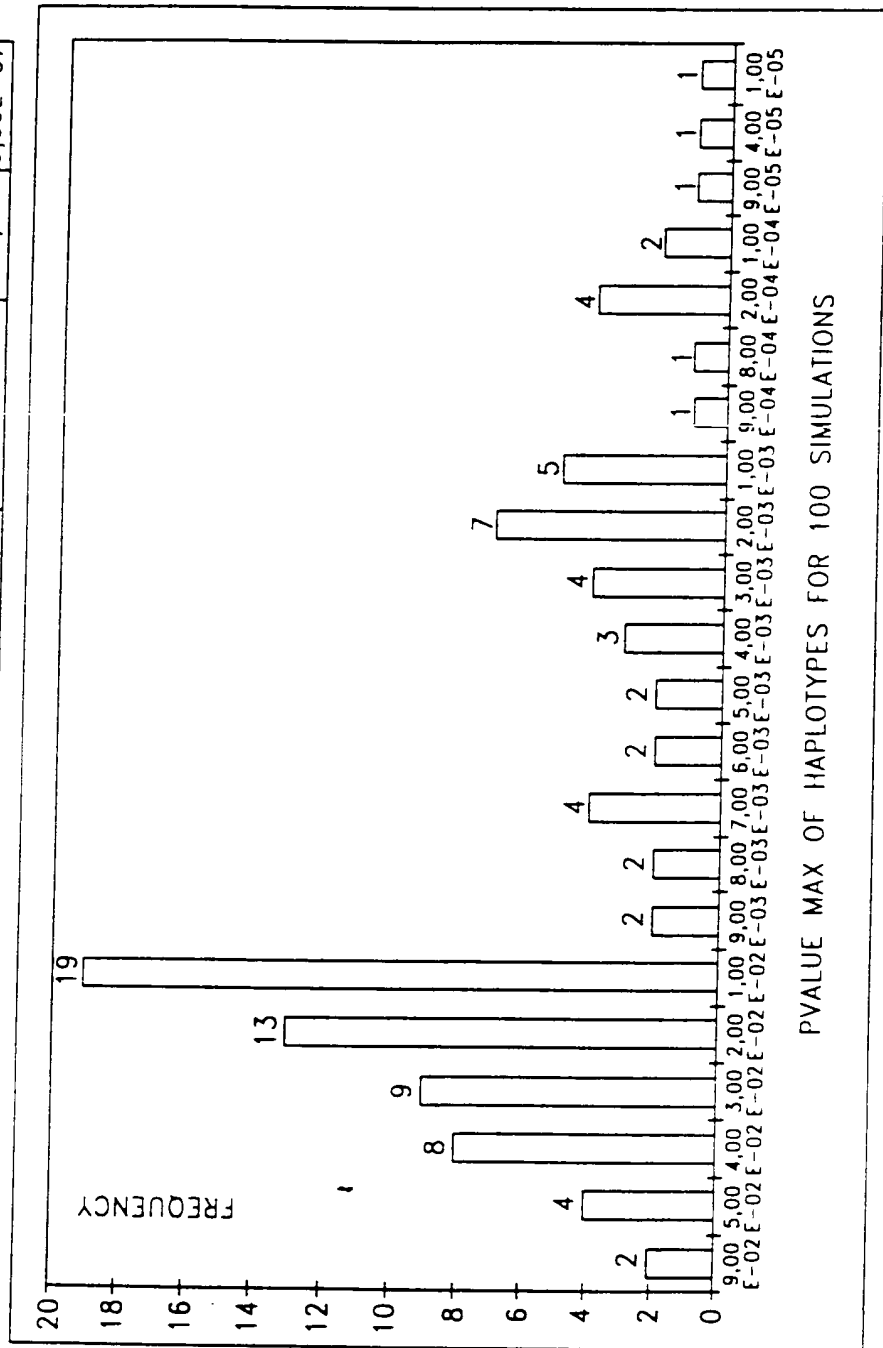
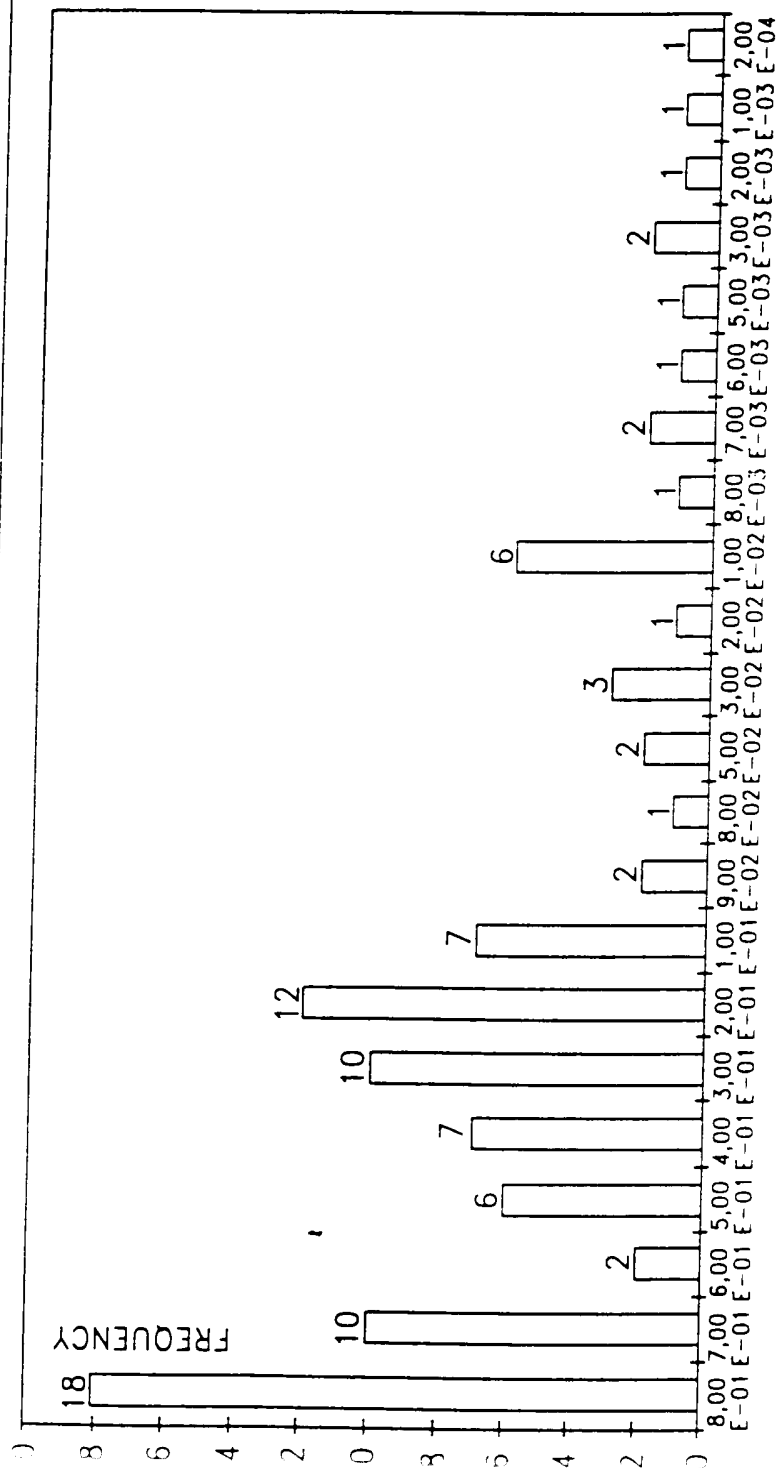


FIG.5A

MARKERS	4-144-7799-2174-6799-21399-221				HAPLOTYPE FREQUENCIES		RELATIVE RISK	PVALUE
	HAPLOTYPE	C	G	T	CASES	CONTROLS		
		C	G	T	0,117	0,013	10,06	9,00E-07



PVALUE OF HAPLOTYPE CGTTGA FOR 100 SIMULATIONS

FIG. 5B

MARKER	SEQ. ID N°	SEQ. ID N° (MUT)	PU SEQUENCE	SEQ. ID N°	RP SEQUENCE	SEQ. ID N°	POLYMORPHISM POSITION*	BASE	MICROSEQ. OLIGOS POSITIONS*
99-123	21	30	AAAGCCAGGACTACAAGG	39	TATTCAGAAAGGAGTGGG	48	24	C/T	1-23 25-47 (COMPLEMENTARY)
4-26	22	31	TACAGCCCTGTAAAGACAC	40	TGAGGACTGCTAGGAAG	49	24	A/G	1-23 25-47 (COMPLEMENTARY)
189	23	32	TCTAACCTCTCATCCAAC	41	GACTGTATCCTTTGATGCAC	50	24	C/T	1-23 25-47 (COMPLEMENTARY)
463	24	33	TGTTGATTACAGGCGGC	42	GGAAGGTACATTCATAG	51	24	G/C	1-23 25-47 (COMPLEMENTARY)
99-217	25	34	GGTGGAAATTTACTATATG	43	GTTTATTTTGTGAGCTTIG	52	24	C/T	1-23 25-47 (COMPLEMENTARY)
463	26	35	AAGTTCACCTTCTCAAGC	44	TGAAAGAGTHTATCTCTGG	53	24	C/T	1-23 25-47 (COMPLEMENTARY)
99-213	27	36	ATACTGGCAGCGTGCTTC	45	TTATGGCCCCACATGCTGAG	54	24	C/T	1-23 25-47 (COMPLEMENTARY)
99-221	28	37	CCCTTTTCTTCACGTGTC	46	TCATTCGCTCTGGCTAGTC	55	24	A/C	1-23 25-47 (COMPLEMENTARY)
99-135	29	38	TGGAAGTTGTATTGCC	47	AAACACCTCCCATTTGTC	56	24	A/G	1-23 25-47 (COMPLEMENTARY)

FIG. 6A

POSITIONS ARE GIVEN RELATIVE TO THE SEQUENCE OF THE CORRESPONDING MARKER (i.e. SEQ ID N° 21-38 AND 57-62)

MARKER	SEQ. ID N°	SEQ. ID N° (MUT)	PU SEQUENCE	SEQ. ID N°	RP SEQUENCE	SEQ. ID N°	POLYMORPHISM POSITION*	BASE	MICROSEQ. OLIGOS POSITIONS*
463	57	60	ATCAATCAGTGAAGTCTGAG	63	ACAAATCTATATAAGGCTGG	66	24	A/C	1-23 25-47 (COMPLEMENTARY)
99-1482	58	61	ATCGCTGGAAACATTCTGG	64	CTCTTGGTTAAACAGCAGTG	67	24	G/C	1-23 25-47 (COMPLEMENTARY)
4-73	59	62	GATTTAAGCTACGCTATTAG	65	TGGCTCTGCAATTTCTTCC	68	24	C/T	1-23 25-47 (COMPLEMENTARY)

FIG. 6B

POSITIONS ARE GIVEN RELATIVE TO THE SEQUENCE OF THE CORRESPONDING MARKER (i.e. SEQ ID N° 21-38 AND 57-62)

EXON Phase	START	END	5' SPsite	PHASE	3' SPsite
Ex1 +0	2001	2216			GTGAGC
Ex2 +1	18196	18265	TAG	+0	GTTTGTA
Ex3 +0	23717	23832	CAG	+2	GTAACCT
Ex4 +0	25571	25660	CAG	+0	GTAAGA
Ex5 +2	34669	34759	CAG	+0	GTAAGT
Ex6 +1	40688	40846	TAG	+1	GTAAGT
Ex7 +2	48070	48193	TAG	+2	GTGAGT
Ex8	50182	54523	TAG	+1	
ATG codon	2031	2033			
STOP codon	50405	50407			
POLY Ad site	54445	54450			

FIG. 7

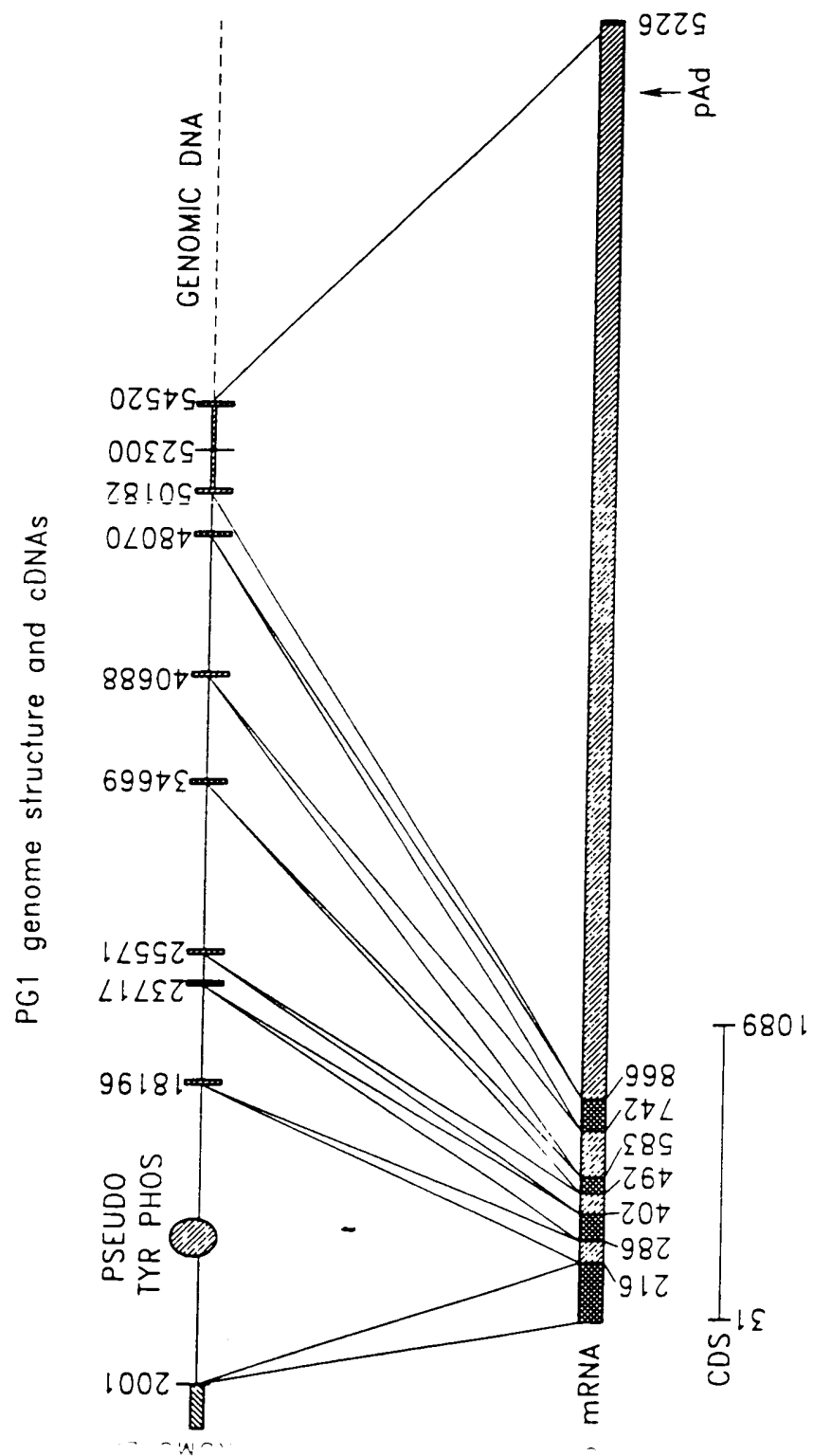
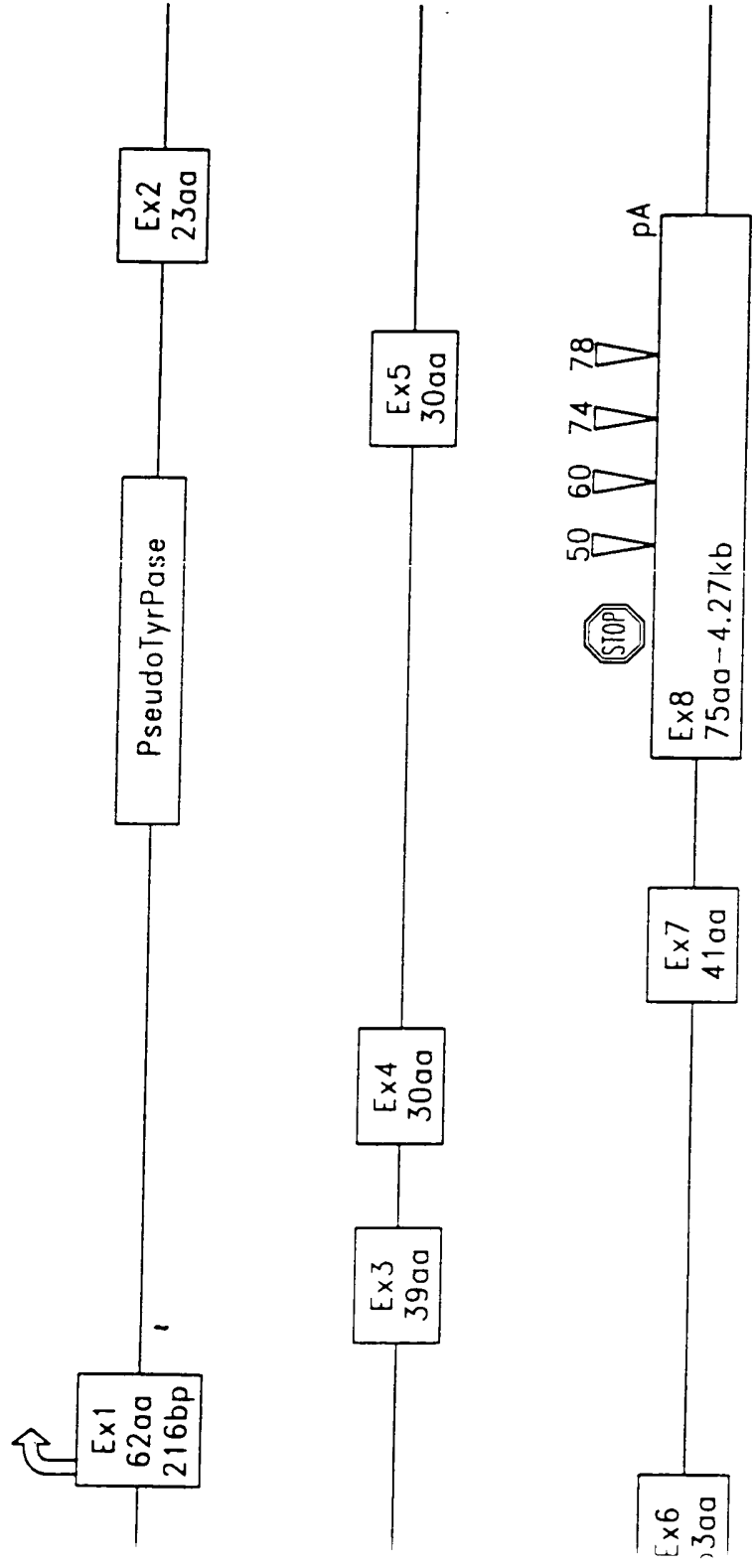


FIG.8

Fig. 8B

Prostate Gene 1



		box 1	box 2	box 3
PG1	Hs	NHQ 81-83	FPEGTR 160-165	LDAIYDVTV 211-219
AF003136 (Genbank)	Ce	NHQ 630-632	FPEGTR 712-717	LDAIYDVTV 762-770
Z72511 (Genbank)	Ce	48 NHR 50	FPEGTD 129-134	VEYIYDITI 204-212
P38226 (Swissport)	Sc	111 NHQ 113	FPEGTN 223-228	IESLYDITI 271-279
P33333 (Swissport)	Sc	81 NHQ 83	FPEGTR 154-159	-
Z49770 (Genbank)	Sc	116 NHQ 118	FPEGTN 215-220	LDAIYDVTI 265-273
P26647 (Swissport)	Ec	72 NHQ 74	FPEGTR 145-150	-
Z49860 (Genbank)	Bn	-	FVEGTR 90-95	VPAIYDMTV 138-146
U89336 (Genbank)	Hs	95 NHQ 97	FPEGTR 168-173	-
U56417 (Genbank)	Hs	103 NHQ 105	FPEGTR 176-181	-
AB005623 (Genbank)	Mm	100 NHQ 102	FPEGTR 173-178	
Z29518 (Genbank)	Zm	91 NHR 93	FVEGTR 170-175	VPAIYDTTV 218-226

Hs = Homo sapiens, Ce = Caenorabibitis elegans, Ec = Escherichia coli;
 Sc = Saccharomyces cerevisiae, Bn = Brassica napus, Zm = Zea maize,
 Mm = Mus Musculus

- = pattern absent from protein sequence

Note: Functional acyl glycerol transferases all contain boxes 1 and 2 and not box 3. Proteins most related to PG1 contain the 3 boxes with a high degree of conservation.



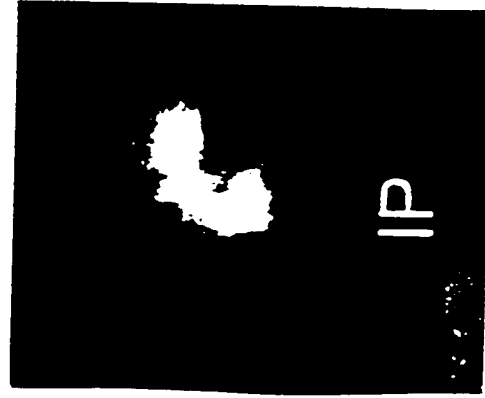
PC3
PG1



PNT2
PG1



FIG. 10

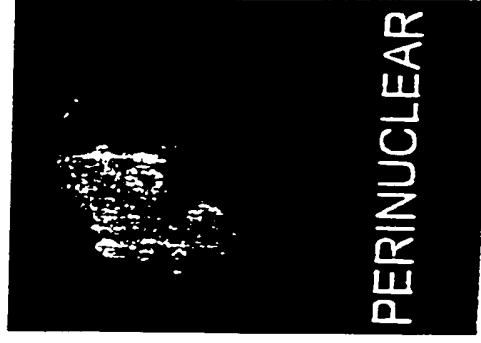


IP



GFP

PC3
PG1
1-4



PERINUCLEAR

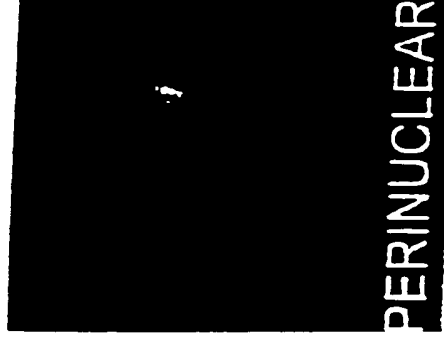


IP



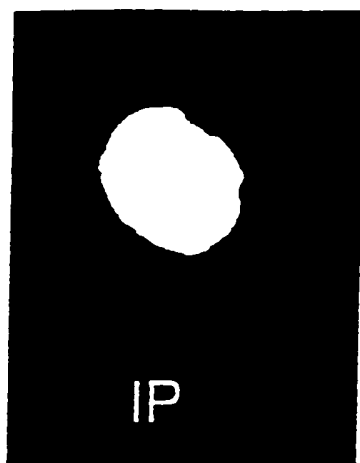
GFP

PNT2
PG1
1-4

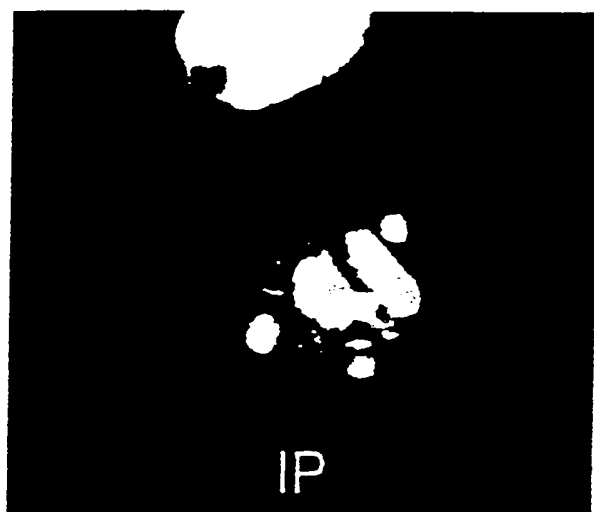
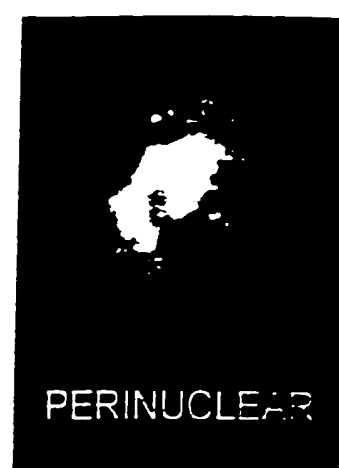


PERINUCLEAR

FIG. 11



PC3
PG1
1-5



PNT2 PG1 1-5

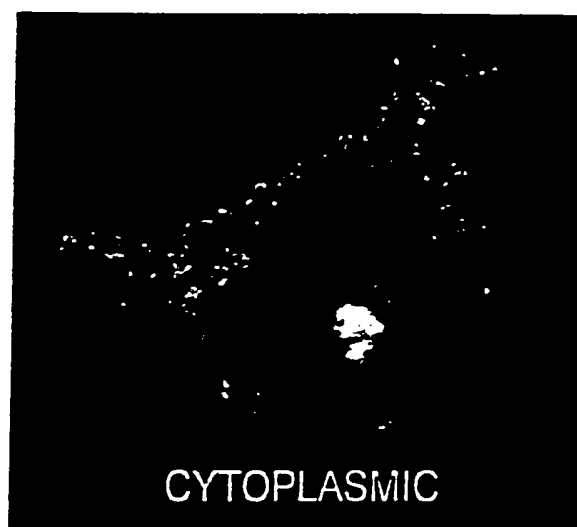
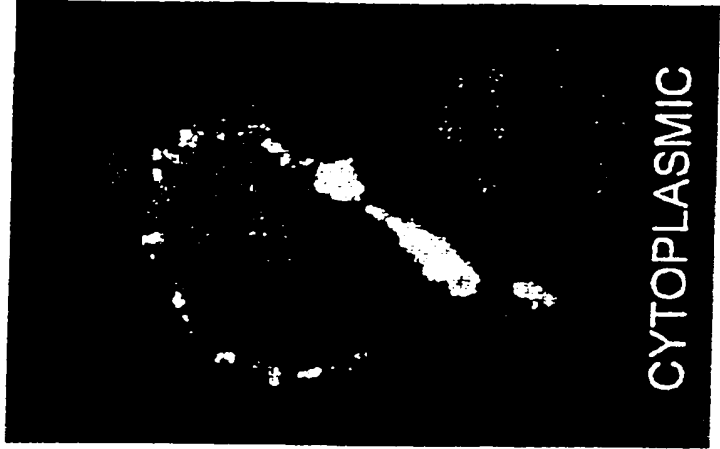
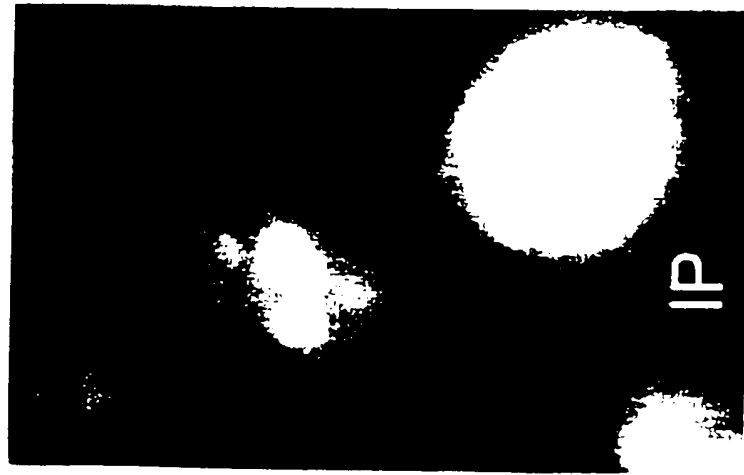


FIG. 12



PNT2 PG1 mut229

FIG. 13

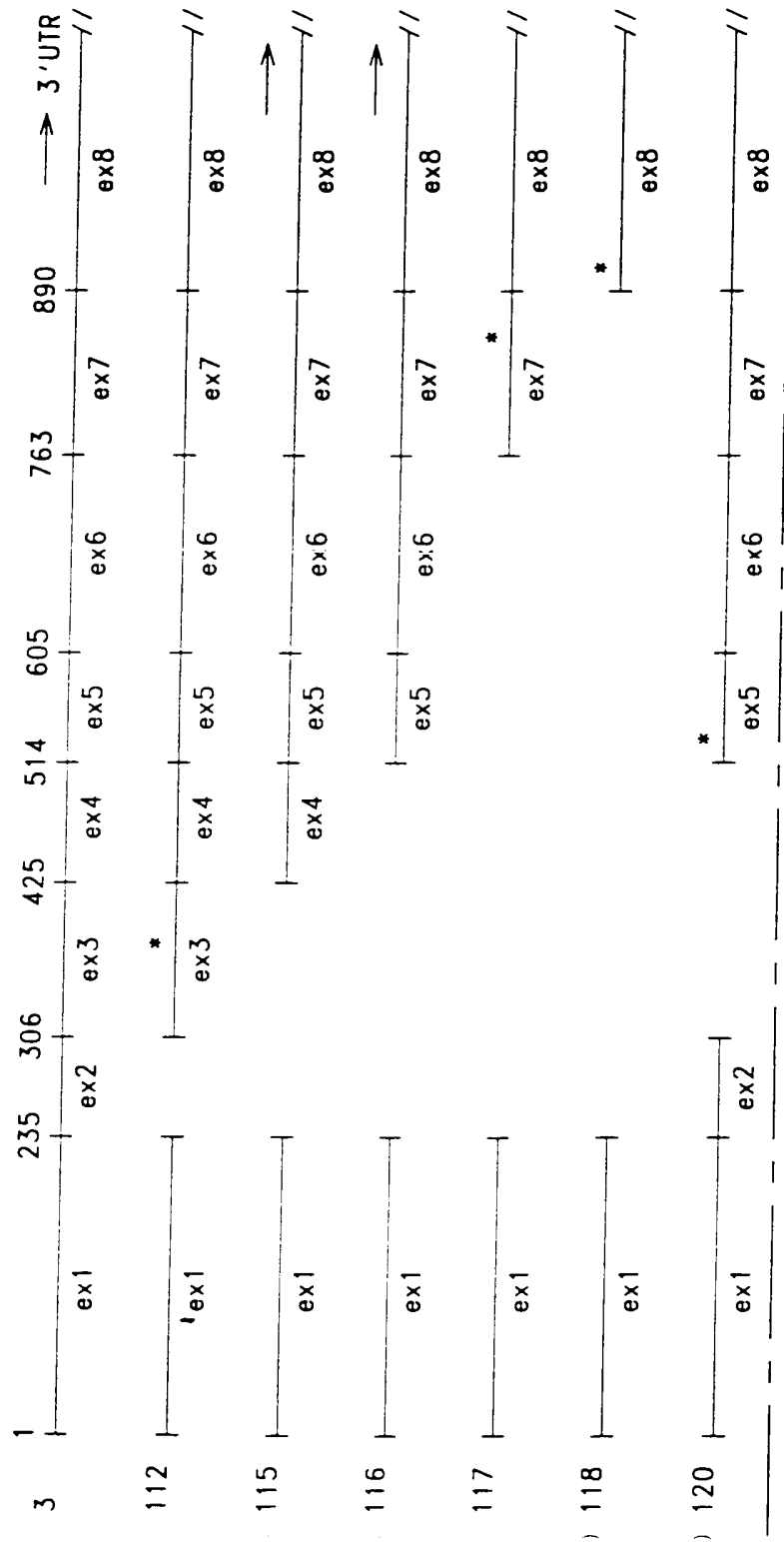
FIG. 14A

FIG. 14

FIG. 14A

FIG. 14B

Alternative splicing



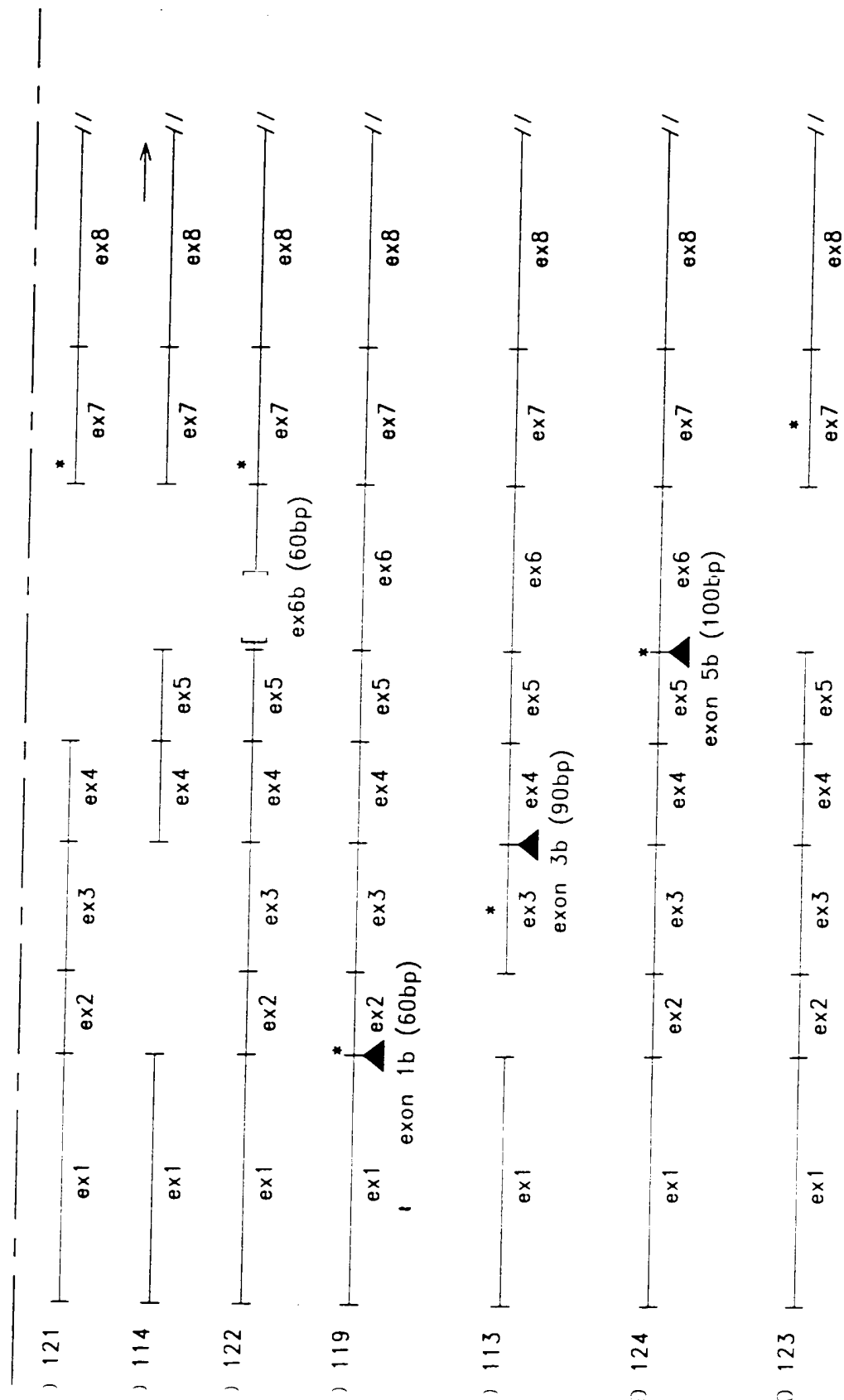


FIG. 14B

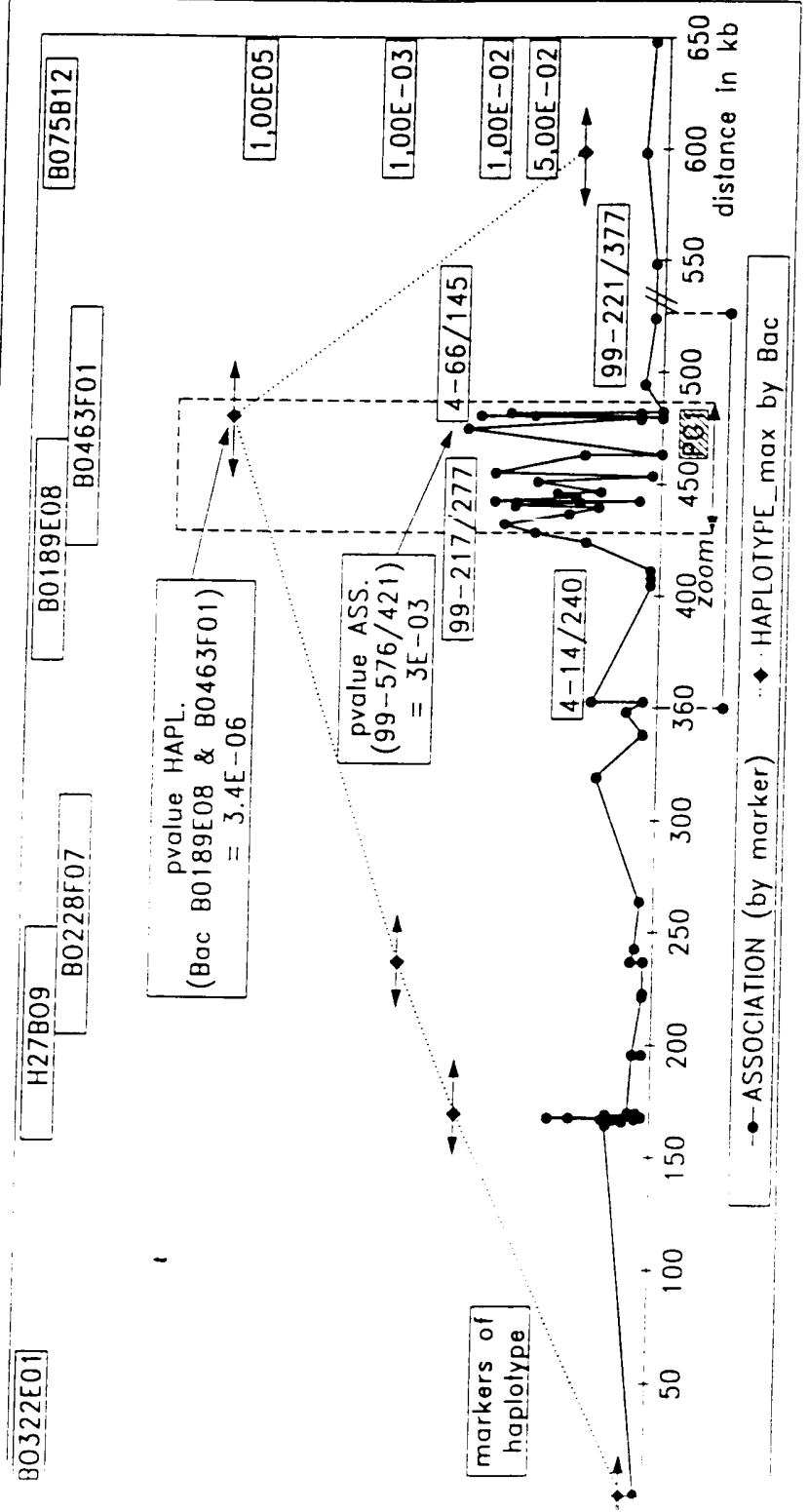
Combination of exons of PG⁺ gene discovered by PCR with primers specific for exon borders

[illegible]

[+] alternative splicing form with combination of exons 13478 instead of 1345678

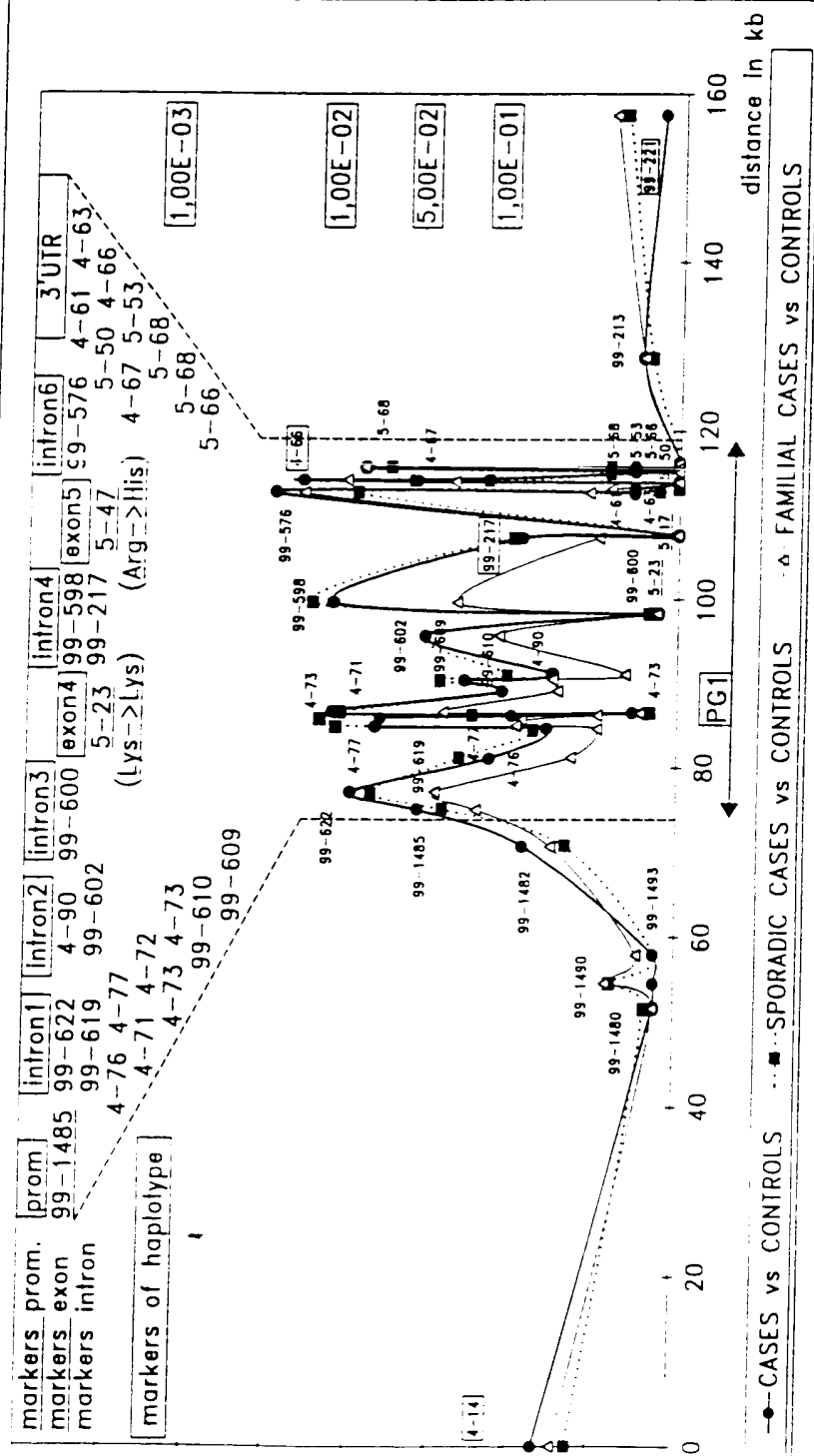
ASSOCIATION STUDIES HAPLOTYPE FREQUENCY ANALYSIS (chrom 8p23)

POPULATIONS	AFFECTED N = [275;491]	UNAFFECTED N = [130;313]
	ALL CASES	CONTROLS
characteristics of populations	[275,491] all cases	<28 unaffected (65 years or older) & <289 controls (65 years or older with PSA<4)



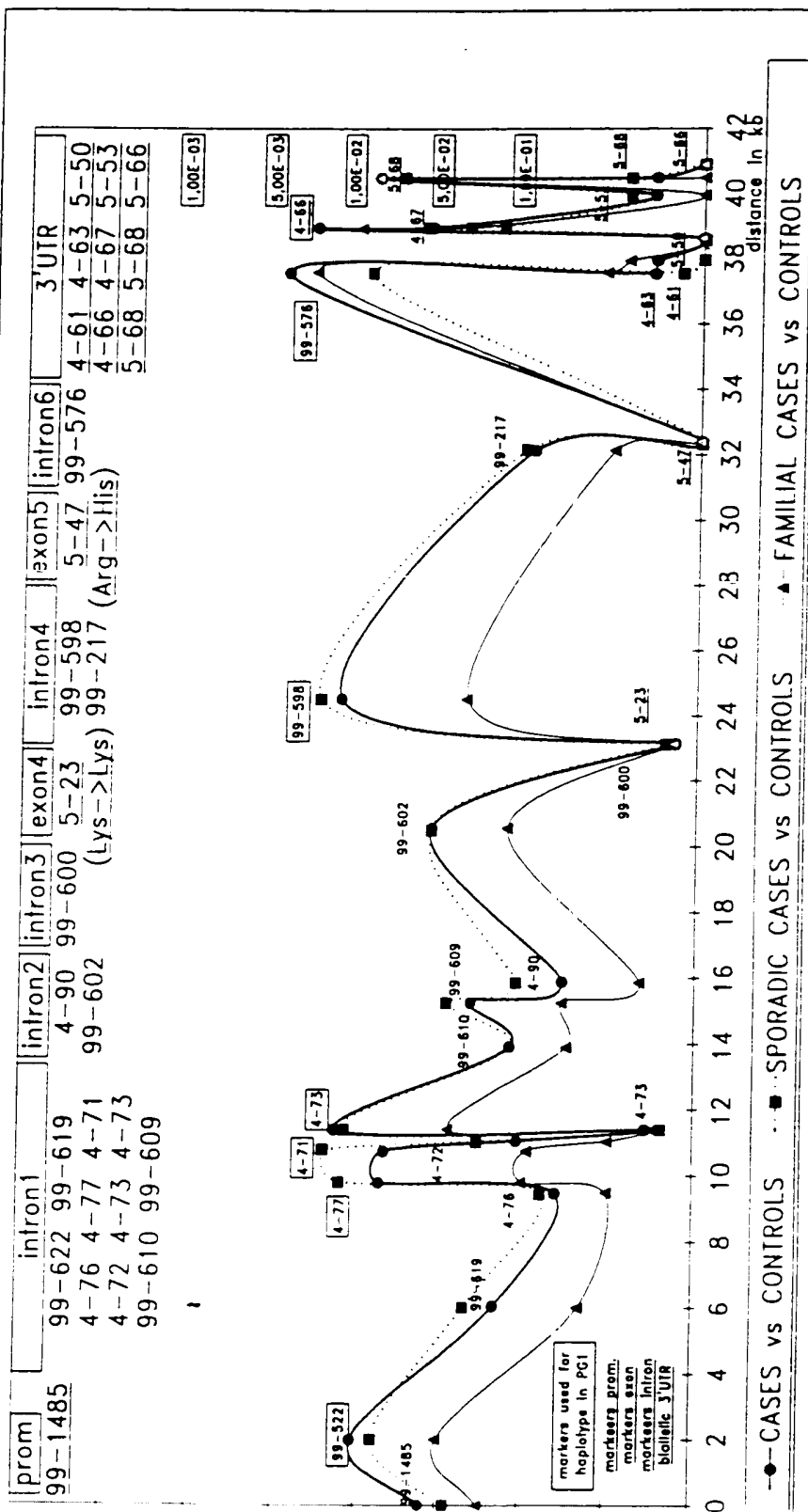
ASSOCIATION STUDIES PG1 (8p23)

ACTIONS	AFFECTED N= [275;491]			UNAFFECTED N=[130;313]	
	ALL CASES	SPORADIC CASES	FAMILIAL CASES	CONTROLS	
teristics ulations	<=491 all cases	<=294 sporadics cases	<=197 familial cases	<28 unaffected (65 years or older) & <=289 controls (65 years or older with PSA<4)	



PG1 (8p23)

ACTIONS	AFFECTED N= [275;491]			UNAFFECTED N=[130;313]
	ALL CASES	SPORADIC CASES	FAMILIAL CASES	
characteristics mutations	<=491 all cases	<=294 sporadics cases	<=197 familial cases	<28 unaffected (65 years or older) & <=289 controls (65 years or older with PSA<4)



no of cases	PG1	Polym.	Freq(cas)	Freq(controls)	abs diff % (fq(cases)-(fq(controls)))	Odd Ratio	Pvalue	Freq(randoms)	Attributable Risk
39 1145/251	prom	G*/T	0.32	0.24	7.4	1.44	2.53E-02	0.29	17.58
39 622/95	in1	G/T	0.52	0.42	10.1	1.51	9.64E-03	ND§	ND
39 614/141	in1	C/T	0.28	0.22	5.8	1.37	6.93E-02	ND	ND
4 612	in1	G/A	0.43	0.38	5	1.23	1.57E-01	0.41	13.15
4 751	in1	G/C	0.34	0.26	7.4	1.43	1.35E-02	0.31	18.16
4 133	in1	A/G	0.34	0.26	8.3	1.49	1.43E-02	0.28	18.64
4 277	in1	A/G	0.36	0.30	5.7	1.29	9.43E-02	0.31	13.25
4 334	in1	G/C	0.52	0.42	9.7	1.48	7.29E-03	0.52	26.76
99 614/250	in1	G/A	0.43	0.37	6.2	1.30	8.33E-02	ND	ND
99 614/225	in1	A/T	0.37	0.30	7	1.36	4.83E-02	ND	ND
4 1083	in2	A/C	0.29	0.25	4.4	1.25	1.68E-01	0.28	9.32
99 614/258	in2	A/G	0.33	0.25	7.4	1.44	2.69E-02	ND	ND
99 614/492	in3	T/A	0.34	0.34	0.3	1.01	7.52E-01	ND	ND
99 614/130	in4	G/A	0.35	0.25	9.2	1.55	7.29E-03	ND	ND
99 614/277	in4	T/C	0.31	0.28	3.8	1.20	1.07E-01	0.28	8.46
99 614/421	in6	G/C	0.27	0.17	9.2	1.72	3.18E-03	0.24	18.40
4 169	3'UTR	G/A	0.01	0.00	0.3	1.76	0.527§	ND	ND
4 145	3'UTR	C/T	0.25	0.19	6.2	1.43	4.68E-03	0.24	13.16
4 145	3'UTR	T/C	0.25	0.20	4.9	1.33	2.39E-02	0.24	10.97

§ Test Fisher-§ ND: Not done -* disease associated allele / not associated allele

FIG. 18B

HAPLOTYPE FREQUENCY ANALYSIS

haplotype frequencies		Odd ratio	Chi-S	Pvalue	
cases	controls				
0.116	0.067	1.83	9.85	(1.7e-03)	***
0.243	0.183	1.43	7.49	(6.2e-03)	**
0.182	0.130	1.49	7.18	(7.3e-03)	**
0.217	0.188	1.20	1.88	(1.7e-01)	*
0.155	0.132	1.20	1.54	(2.1e-01)	*
0.373	0.346	1.12	1.16	(2.7e-01)	*
0.095	0.042	2.39	14.62	(1.3e-04)	*****
0.117	0.065	1.93	11.33	(7.3e-04)	***
0.095	0.032	3.18	21.59	(3.4e-06)	*****

IG. 19B

HAPLOTYPE FREQUENCY ANALYSIS

PG1 (8p23)

markers of haplotype Max	4-14/240	99-217/277 in4	4-66/145 3'UTR	99-221/377
	C	T	C	A
distance between mks	<100kb>		<17kb>	
			<43kb>	

PG1	sample sizes	haplotype frequencies		odd ratio	chi-S	P value
		cases vs control	controls			
control	455 vs 294	0.095	0.032	3.18	21.59	3.40E-06 *****
(≤65 years) vs controls	171 vs 294	0.105	0.032	3.56	20.91	4.60E-06 *****
(>65 years) vs control	271 vs 294	0.079	0.032	2.60	12.13	4.80E-04 ****
cases vs controls	266 vs 294	0.096	0.032	3.23	19.73	8.60E-06 *****
adic cases (≤65 years) vs controls	85 vs 294	0.095	0.032	3.20	12.04	5.00E-04 ****
idic cases (>65 years) vs controls	178 vs 294	0.085	0.032	2.82	12.75	3.50E-04 ****
malive sporadic cases vs controls	67 vs 294	0.062	0.032	2.00	2.70	9.40E-02 **
cases vs controls	179 vs 294	0.098	0.032	3.32	18.33	1.80E-05 *****
al cases (≤65 years) vs controls	86 vs 294	0.112	0.032	3.83	17.98	2.20E-05 *****
al cases (>65 years) vs controls	93 vs 294	0.075	0.032	2.48	6.59	1.00E-02 **
ial cases (>=3 caP) vs controls	79 vs 294	0.123	0.032	4.26	21.33	3.70E-06 *****

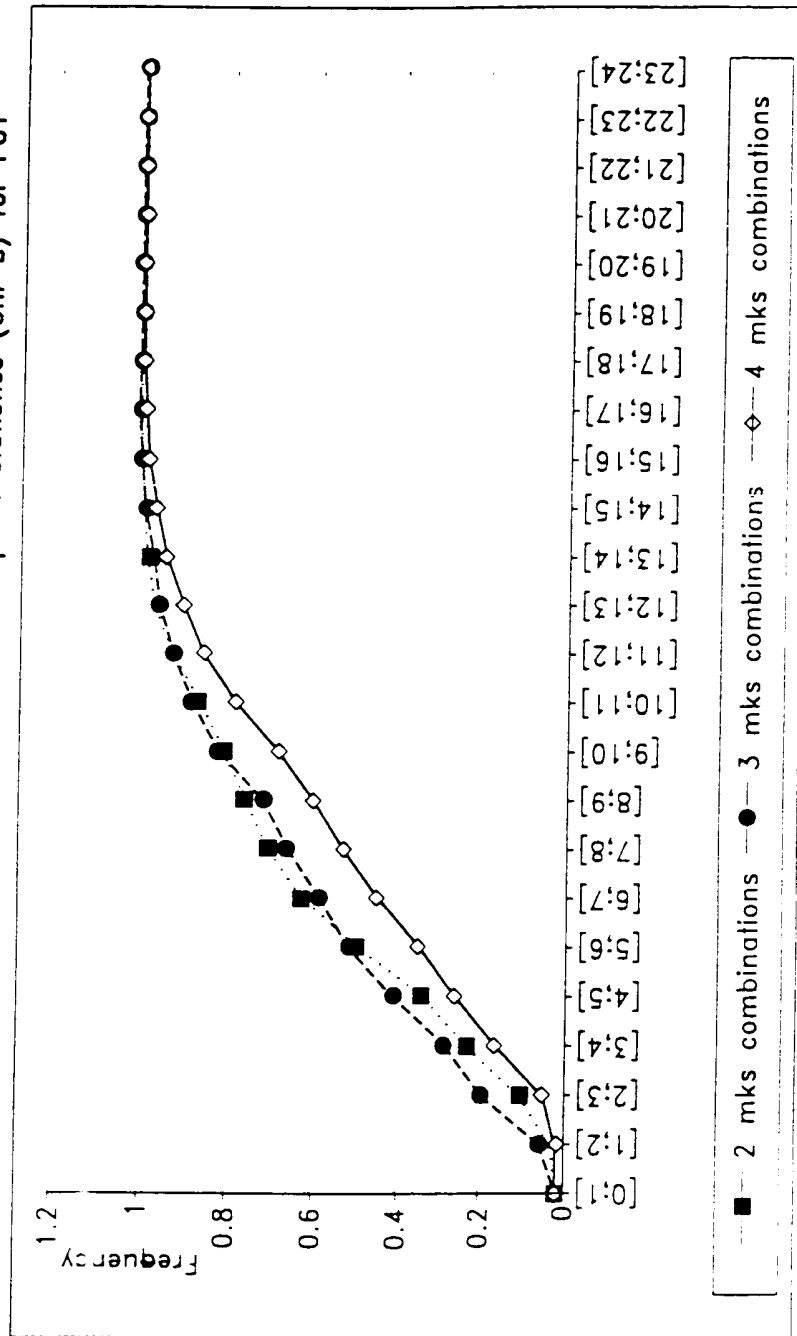
HAPLOTYPE FREQUENCY ANALYSIS (PG1)

Not Done

Comparison of Pvalue between nb of mks for haplotype (19 mks of PG1)

GENE	# of markers	# of 2 mks combinations	# of 3 mks combinations	# of mks combinations
PG1	19	171	969	3876

CUMULATIVE FREQUENCY HISTOGRAM OF Chi-square statistics (Chi-S) for PG1



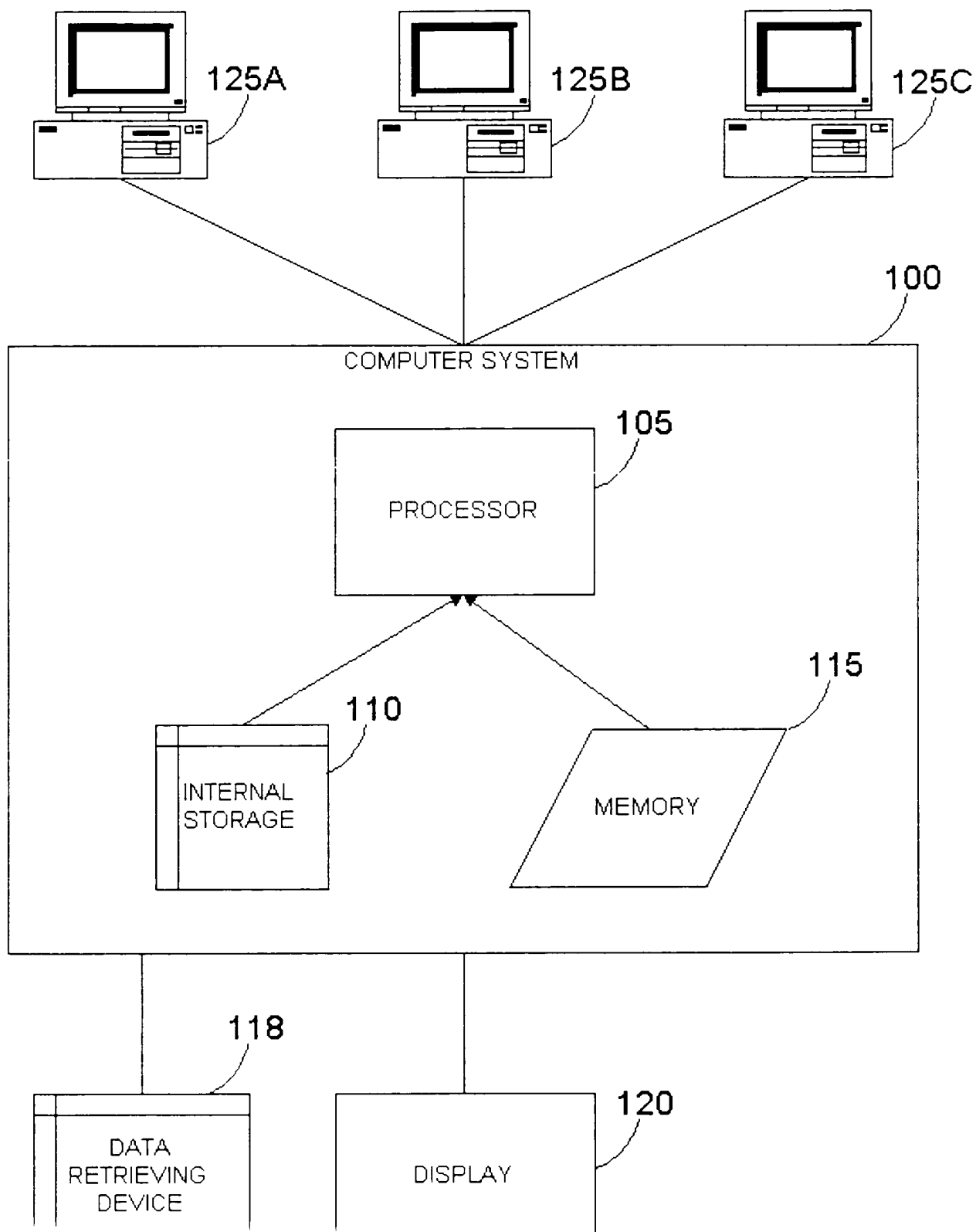


FIG. 22

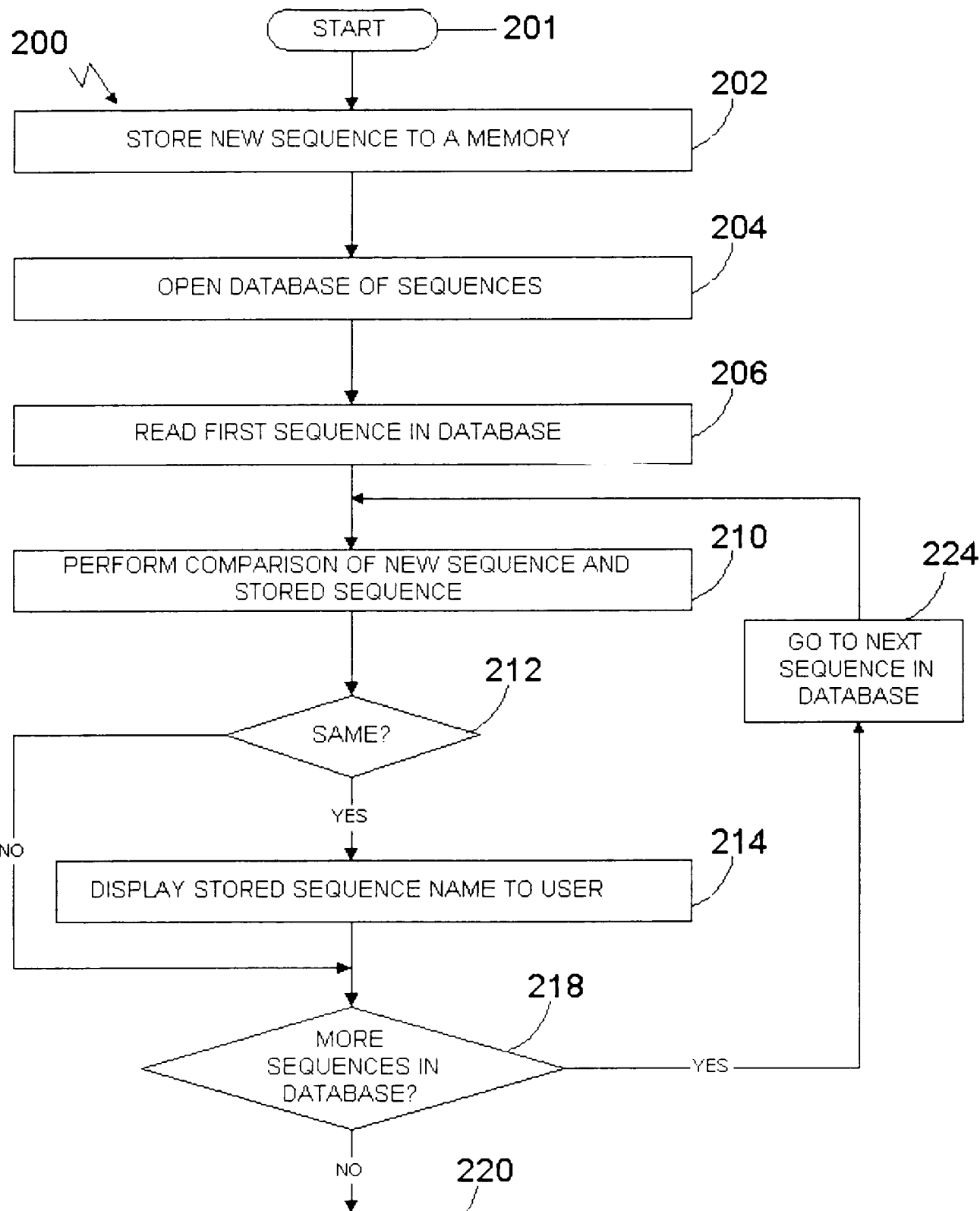


FIG. 20

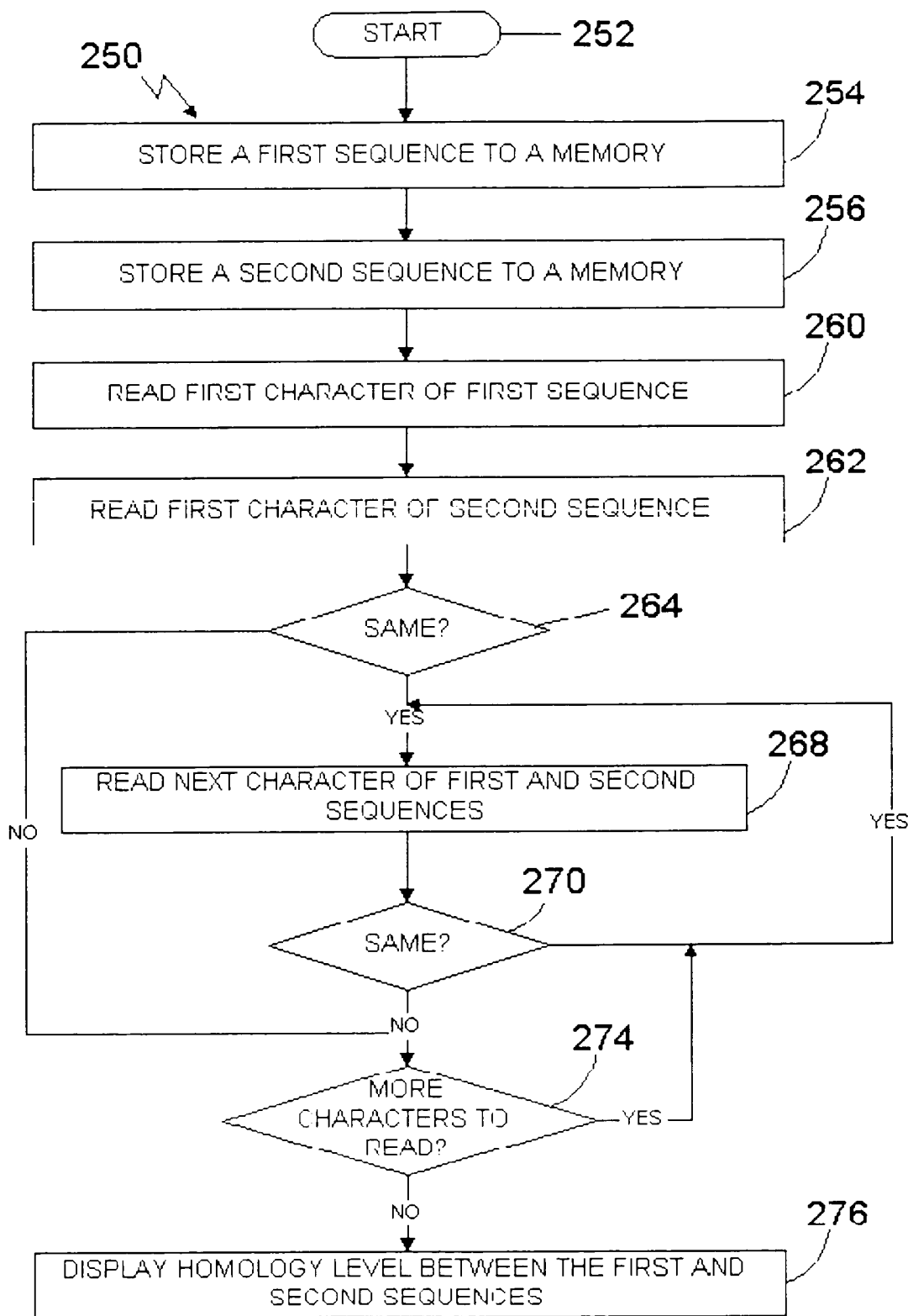


FIG. 24

